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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/510,229

10/13/2004

Yoram Reiter

28429

6861

67801

7590

02/24/2009

MARTIN D. MOYNIHAN d/b/a PRTSI, INC.

P.O. BOX 16446

ARLINGTON, VA 22215

EXAMINER

LUCAS, ZACHARIAH

ART UNIT

PAPER NUMBER

1648

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<i>Office Action Summary</i>	Application No.	Applicant(s)	
	10/510,229	REITER ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2008.
- 2a) ☒ This action is FINAL.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 141-160 and 197-214 is/are pending in the application.
- 4a) Of the above claim(s) 150 and 200-211 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 141-149, 151-160, 197-199, and 212-214 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/27/08 1/4/09</u>  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Claims 141-160 and 197-214 are pending in the application.
2. In the prior action, mailed on June 18, 2008, claims 141-160 and 196-212 were pending; with claims 150 and 200-211 withdrawn from consideration; and claims 141-149, 151-160, and 197, 189, and 212 under consideration and rejected; and claim 199 objected to.
3. In the Response of November 18, 2008, the Applicant amended claims 141 and 199; and added new claims 213 and 214.
4. Claims 141-149, 151-160, 197-199, and 212-214 are under consideration.

#### *Information Disclosure Statement*

5. The information disclosure statements (IDS) submitted on June 27, 2008 and on January 4, 2009 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Reference 4 of the January 2009 IDS is in a foreign language and is not accompanied by an English language translation or indication of the relevance of the reference. The reference has therefore not been considered.

References 65 and 75 of the June 2008 IDS were previously made of record in the IDS of January 2007. These references have therefore been crossed out in the latter IDS.

#### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. (New Rejection- Necessitated by Amendment) Claim 199 is rejected under 35

U.S.C. 112, first paragraph, because the specification, while being enabling for methods of killing or damaging cells if the antibody includes a domain such as that described in lines 6-7 of claim 1, does not reasonably provide enablement for the use of an antibody or fragment thereof capable only of binding the target MHC/peptide complexes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection is on the same grounds as was previously applied in the actions mailed in January 2007 (pages 3-5) and October 2007 (pages 3-5). As amended claim 199 no longer includes the language of claim 1 which was inserted to overcome the rejection, the rejection is reinstated against this claim.

*Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. (Prior Rejection- Maintained) Claims 141-149, 151-155, 158, 159, and 212 were rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter (PNAS 94:4631-36), further in view of the teachings of Andersen et al., (WO 97/02342) and of Chames et al. (PNAS 97:7969-74). The claims have been amended to require that the antibody (or fragment thereof) to which

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the cell is exposed is a soluble antibody. The Applicant has additionally added new claims 213 and 214, which require that the antibodies are obtainable through the use of the soluble MHC complexes as described in the present application. While these two new claims indicate that the antibodies must be obtainable through such methods, there is no structural difference between antibodies that are so obtained, and antibodies that may be obtained through other antibody screening methods. Nor do the claims actually require the use of the disclosed screening methods for the production of such antibodies. The rejection is therefore extended to claims 213 and 214.

Applicant continues to traverse the rejection on the basis that the presently claimed inventions provide unexpected results over the teachings of the cited prior art. The arguments are not found persuasive.

The Applicant first asserts that the teachings of Chames cannot be applied to the arts of Andersen and Reiter because the antibodies identified in the reference were low affinity binders which could not bind cells in their soluble forms. While this may be the case with respect to the specific antibody described by the reference, the reference nonetheless teaches that the methods disclosed therein may be used to isolate and identify antibodies with the desired binding specificity.

Further, the reference itself indicates that tumor antigens, the class of antigens being used in the reference, are often unable to elicit an adequate immune response. This is not a problem that those of ordinary skill in the art would have considered to apply equally to antigens from pathogens in view of the fact that tumor antigens were known to be self antigens, whereas antigens from pathogens were known to be foreign antigens. Moreover, while the Applicant has noted that the use of the methods for isolating the antibodies described in the present application

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did achieve higher numbers of antibodies than were expected, the teachings in the art indicates that this is evidence of the quality of the phage libraries being screened, and not a result of the use of the soluble MHC complexes described in the present application. See e.g., Lev et al., *Cancer Res* 62:3184-94, at 3193 (reference of record in the June 2008 IDS). Lev also indicates that the surprisingly high frequency of such antibodies identified in methods such as those described in the present application (see, Lev, page 3185, indicating that soluble MHC complexes were also used in this reference) has more to do with the surprisingly high frequency of such antibodies in donors of the phage library than with the methods used to screen the library.

Finally, it is noted that the Applicant's arguments with respect to the indicia of non-obviousness are directed to the methods used to isolate the antibodies. However, while the arguments indicate that the disclosed means for producing such antibodies may be more successful than those suggested by the prior art, even the teachings of the Lev reference indicate that the screening methods of Chames (i.e. the use of phage display screening) is a powerful selection tool. Lev, page 3193. Thus, the teachings in the art indicate that, even if the use of the soluble MHC complexes described in the present application are more efficient in the identification of such antibodies, the methods of Chames and the other previously cited references would still be capable of identifying antibodies that could be used as suggested by Reiter and Andersen.

With respect to the inability of the antibody of Chames to perform as required by the claims, it would have been apparent to those of ordinary skill in the art that further screening would be required to identify antibodies that target the desired complexes with adequate affinity

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to be capable of use in the methods suggested by Reiter and Andersen. Having identified such antibodies according to the methods suggested by the prior art, it would have been obvious to those of ordinary skill in the art use the antibodies (or fragments thereof) as described by the claims, and suggested by Reiter and Andersen.

Because the present claims are not drawn to methods for the isolation of such antibodies, but to methods for the use of the antibodies once they have been isolated, and as the art suggests the identification and such uses of the antibodies, the Applicant's arguments are not found persuasive. The arguments presented are not directed to the invention being claimed, but to the use of antibodies that may be identified through the use of the possibly improved screening methods described by the present application, but which methods are not part of the claimed invention.

The rejection is therefore maintained for the reasons above, and the reasons of record.

10. (Prior Rejection- Maintained) Claims 141-149, 151-159, and 212 were rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter in view of Andersen and Chames as applied above, further in view of the teachings of Matsushita et al. (U.S. 5,591,829). As no additional arguments were made with respect to this rejection over those asserted to the rejection over Reiter in view of Andersen and Chames, the rejection is maintained over such arguments for the reasons indicated above, and is extended to new claims 213 and 214.

11. (Prior Rejection- Maintained) Claims 141-149, 151-160, and 212 were rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter in view of Andersen and Chames as applied

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above, further in view of the teachings of Saito et al. (J Virol 75: 1065-71). As no additional arguments were made with respect to this rejection over those asserted to the rejection over Reiter in view of Andersen and Chames above, the rejection is maintained over such arguments for the reasons indicated above, and is extended to new claims 213 and 214.

12. (Prior Rejection- Maintained) Claims 141-149, 151-155, 158, 159, 197, 198, and 212 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter in view of Andersen and Chames as applied above, further in view of Carter et al. (U.S. 6,054,297). As no additional arguments were made with respect to this rejection over those asserted to the rejection over Reiter in view of Andersen and Chames above, the rejection is maintained over such arguments for the reasons indicated above, and is extended to new claims 213 and 214.

13. (New Rejection- Based on reference cited in an IDS) Claims 141-149, 151-155, 158, 159, and 212-214 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lev et al., (Cancer Research 62:3184-94- of record in the June 2008 IDS) in view of the teachings of Reiter and Andersen. The teachings of Lev are similar to those of the previously applied Chames reference, except that the reference teaches the use of the soluble MHC complexes used in the screening methods of the present application. The reference also teaches the surprisingly frequent identification of antibodies with the desired function properties from phage libraries. It would therefore have been obvious to those of ordinary skill in the art to have used such antibodies in the methods suggested by Reiter and Andersen as previously described.

Moreover, because Lev teaches methods of screening for antibodies that results in the same surprisingly frequent incidence of the functional antibodies as asserted by the application with respect to the methods disclosed in the application, Applicant's arguments are not found persuasive with respect to this rejection.

14. (New Rejections- Based on reference cited in an IDS) Claims 141-149, 151-160, 197, 198, and 212-214 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lev et al., (Cancer Research 62:3184-94) in view of the teachings of Reiter and Andersen as applied above; and further in view of the teachings of Matsushita, Saito, and Carter as applied previously against the limitations of claims 156 and 157; claims 156, 157, and 160; and claims 197 and 198, respectively. Each of claims 156, 157, 160, 197, and 198 provide for limitations not met by the teachings of Lev in view of Andersen and Reiter. However, such limitations are suggested by the teachings of the additional references as previously described. The claims are therefore rendered obvious by these references for the reasons indicated with respect to the teachings of Lev, Andersen, and Reiter as applied above, and the additional references as previously described.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

### *Double Patenting*

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. (Prior Rejection- Maintained) Claims 141-149, 151-160, 197, and 198 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8, 11, and 13 of copending Application No. 11/629194, or the copending claims in view of the teachings of Reiter, Chames, and Andersen and any of Matsushita, Saito, or Carter as described above. As it is not Office policy to hold the rejection in abeyance, the rejection is maintained. The rejection is also extended to new claims 213 and 214.

### *Conclusion*

18. No claims are allowed.

19. The new rejections presented in the above action were either necessitated by Applicant's amendment of the claims, or prompted by Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on June 27, 2008.

Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/

Primary Examiner, Art Unit 1648